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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TURNER, SHARON L	

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 04/05/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/836,960	CEN ET AL.	
	Examiner	Art Unit	
	Sharon L. Turner	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *14 January 2004*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *23-37* is/are pending in the application.

4a) Of the above claim(s) *26,28-32 and 35-37* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *23-25,27,33 and 34* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *23-37* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *14 January 2004* is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☒ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Response to Amendment

1. The amendment and drawing filed 1-14-04 have been entered into the record and have been fully considered.

2. The text of Title 35 of the U.S. Code not reiterated herein can be found in the previous office action.

3. As a result of Applicant's amendment, all rejections not reiterated herein have been withdrawn by the examiner.

Priority

4. Applicant has not complied with one or more conditions for receiving the benefit of an earlier filing date under 35 U.S.C. 119(e) as follows:

The later-filed application must be an application for a patent for an invention which is also disclosed in the prior application (the parent or original nonprovisional application or provisional application); the disclosure of the invention in the parent application and in the later-filed application must be sufficient to comply with the requirements of the first paragraph of 35 U.S.C. 112. See *Transco Products, Inc. v. Performance Contracting, Inc.*, 38 F.3d 551, 32 USPQ2d 1077 (Fed. Cir. 1994).

Instant application claims benefit based upon the disclosures of 60/077,411, 60/083,553 filed 3-9-1998 and 4-29-1998, respectively, PCT/US99/05235 filed 3-9-99 and 09/264,851 filed 3-8-99. However, the Examiner fails to find support for the newly claimed "method for supporting the growth and/or survival of precursor cells of the nervous system ex vivo, said method comprising removing said cells from a patient suffering from a condition capable of treatment with a neurotrophic factor administering

to said cells from said patient a composition comprising an isolated polypeptide consisting of a polypeptide encoded by SEQ ID NO:4 and transplanting or engrafting said cells to said patient." In particular support is not found for generic growth and/or survival of precursor cells of the nervous system ex vivo. Moreover, support is not found for removing such cells from a patient suffering from the particular condition, administering to the cells the polypeptide and transplanting and engrafting the cells back to said patients, in particular with Parkinson's or ischemic stroke as claimed. The provisional applications are further noted to lack the disclosure of Examples 6 and 7 exhibiting neuronal stem cell proliferation. Thus, the priority applications fail to provide support and enablement for the invention as instantly claimed and the priority dates cannot be granted absent evidence for enabling disclosure within the provisionals. The effective filing date of instant claims is the instant filing date of 09/836,960 filed 4-17-01.

Applicants argue in the response of 1-14-04 that their amendments to the claims obviate the rejection.

Applicant's arguments filed 1-14-04 have been fully considered but are not persuasive. Applicant's new recitations are unsupported within the noted priority documents. In order to obtain benefit of the priority dates, Applicants are required to point to support within the priority applications, by page and line number, where such support may be found.

Election/Restriction

5. Applicant's election with traverse of Group I, claims 23-29, species (C) Parkinson's Disease in Paper No's. 8 and 12 is acknowledged. Because applicant did

not distinctly and specifically point out the supposed errors in the restriction requirement, the election has been treated as an election without traverse (MPEP § 818.03(a)).

Claims 26 and 28-32 are withdrawn from further consideration pursuant to 37 CFR 1.142(b) as being drawn to nonelected species, there being no allowable generic or linking claim. Election was made **without** traverse in Paper No's 8 and 12. Claim 27 will be examined based upon it's inclusion in the prior art found and cited herein by the Examiner in the search of the elected invention.

6. Newly submitted claims 35-37 are directed to an invention that is independent or distinct from the invention originally claimed for the following reasons: The method newly recites a method for treating Parkinson's disease comprising administration of a polypeptide encoded by SEQ ID NO:4. The method thus is drawn to a new method of treatment that differs in treatment of Parkinson's and particular contacting steps. Thus the claims are patentably distinct and require new search and consideration on the merits.

Since applicant has received an action on the merits for the originally presented invention, this invention has been constructively elected by original presentation for prosecution on the merits. Accordingly, claims 35-37 are withdrawn from consideration as being directed to a non-elected invention. See 37 CFR 1.142(b) and MPEP § 821.03.

7. This application contains claims 26, 28-32 and 35-37 drawn to an invention nonelected with traverse in Paper No's: 8 and 12. A complete reply to the final rejection

must include cancellation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Claim Rejections - 35 USC § 112

8. The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

9. Claims 23-25, 27 and 33-34 are rejected under 35 U.S.C. 112, first paragraph, as failing to comply with the written description requirement. The claims contain subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention. This is a new matter rejection.

The amendment of 1-14-01 amended the originally presented claims and introduced new claims 23-25, 27 and 33-34 drawn to "A method for supporting the growth and/or survival of precursor cells of the nervous system ex vivo, said method comprising removing said cells from a patient suffering from a condition capable of treatment with a neurotrophic factor, administering to said cells from said patient a composition comprising an isolated polypeptide consisting of a polypeptide encoded by SEQ ID NO:4 and transplanting or engrafting said cells to said patient."

Applicant's point to support for their new recitations at pp. 6, lines 11-21, Example 6 at pl 36 and Example 3, pp. 32-33. However, the Examiner notes that p. 6, lines 11-21, and Examples 3 and 6 fail to provide support for the new recitations. In

particular "growth" is not apparently supported while the specification does apparently speak to expansion or proliferation of neural progenitor/precursor/stem cells in vitro. Moreover, Applicant's amendments with respect to "removing said cells from a patient suffering from a condition capable of treatment with a neurotrophic factor, administering to said cells from said patient a composition comprising an isolated polypeptide consisting of a polypeptide encoded by SEQ ID NO:4 and transplanting or engrafting said cells to said patient" are apparently unsupported by the specification as originally filed. Thus, the recitations constitute new matter absent evidence for support. It is noted that Example 3 is not representative of nervous system cells, but to granulose cells and further that Example 6 is representative only of stem cell proliferation, increased number of neural cells and increased survival in comparison to bFGF.

10. Claims 23-25, 27 and 33-34 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for providing increased neuronal stem cell proliferation from cultured embryonic rat hippocampus as exemplified in Examples 6-7, does not reasonably provide enablement for supporting the growth and/or survival of precursor cells of the nervous system ex vivo, said method comprising removing said cells from a patient suffering from a condition capable of treatment with a neurotrophic factor, administering to said cells from said patient a composition comprising an isolated polypeptide consisting of a polypeptide encoded by SEQ ID NO:4 and transplanting or engrafting said cells to said patient as claimed

The specifications disclosure is insufficient to enable one skilled in the art to practice the invention as broadly claimed without undue experimentation.

The specification is limited to the exemplification of neural stem cell proliferation as exemplified in Examples 6 and 7 involving cultures of rat embryonic hippocampus. Thus, the specification provides enablement for these effects in neural stem cells but not for growth per se which is recognized generally in the provision of neurite extension.

With respect to the recitations of providing growth and survival to cells from a patient, wherein the patient suffers from Parkinson's, Alzheimer's, stroke, brain injury or spinal cord injury, the specification does not teach that FGF98 provides for growth of such cells from human patients or to subsequent transplantation or engraftment of FGF98 expanded neuronal precursor cells to such patients. Such recitations are akin to autologous expansion and engraftment. However, as noted by Liu, J. of Hematotherapy & Stem Cell Research 2003 Dec 12(6):689-99 and Goh, J. of Hematotherapy & Stem Cell Research 2003 Dec 12(6):671-79 such methodology is a focus of current research for which standard uses are not currently recognized. Even in 2003 such uses are only now being explored let alone being standard at the time of Applicant's invention. Indeed as noted in the new matter rejection as set forth above, the specification fails to teach such methodology as claimed. The specification only provides that isolated neural stem cells from embryonic rat brains cultured *in vitro* exhibit enhanced proliferation following incubation with FGF98. Moreover, these cells are not noted to be of a diseased state and there is no evidence to support the conclusion that such treatment would be effective in cells from a patient in a diseased state.

The skilled artisan recognizes that the neuronal stem/progenitor cells as exemplified in the specification are not mature and/or differentiated adult neurons as in

a patient, see in particular abstract, Florenes et al., Cancer Research, 54(2):354-56, 1994 and abstract, Zimmerman et al., Neuron, 12(1):11-24, 1994 which cumulatively teach differences between neural progenitor cells and neurons as exemplified by nestin expression in proliferating neural stem cells, down-regulation in postmitotic neurons and an absence of such expression in adult brain. Further, it is noted that nestin positive stem cell precursors do not necessarily develop into neurons, but are hallmarks of cancer cells, myocytes, and neuroepithelial cells including oligodendrocytes and glia, see in particular abstract, Florenes et al., abstract Zimmerman et al., as set forth above, and abstract, Gallo et al., J. of Neuroscience 15(1 Pt. 1):394-406, 1995. Thus, the increased proliferation of cells as measured via Nestin expression in Examples 6 and 7 does not appear to be particular to neuronal cells as claimed.

Further, as noted by Hoshikawa et al., Br. Res. Mol. Br. Res., 105(1-2):60-66, 2002 FGF-18 (identical to instant FGF98) is not observed to exhibit neurotrophic activity, recognized as proliferation and growth in cultured rat cortical neurons.

These cumulative teachings indicate that increased expansion/proliferation of neural stem cell precursors as exemplified in Examples 6-7 and Figure 10 of the specification does not provide a basis for supporting the growth and/or survival of precursor cells of the nervous system ex vivo, said method comprising removing said cells from a patient suffering from a condition capable of treatment with a neurotrophic factor, administering to said cells from said patient a composition comprising an isolated polypeptide consisting of a polypeptide encoded by SEQ ID NO:4 and transplanting or engrafting said cells to said patients in diseased states such as Parkinson's, and stroke

as recited in the claims.

The skilled artisan would be forced into further experimentation to determine if the factor is able to provide such support utilizing removed adult neuronal precursors from a diseased patient and further transplanting or engrafting the noted cells.

Thus, in view of the quantity of experimentation necessary, the lack of working examples, the unpredictability of the art, the lack of sufficient guidance in the specification and the breadth of the claims, it would take undue experimentation to make and use the claimed invention.

Status of Claims

11. No claims are allowed.

Conclusion

12. Applicant's amendment necessitated the new ground(s) of rejection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later

than SIX MONTHS from the date of this final action.

13. The Examiner notes that Deisher is withdrawn with respect to the newly recited claims. However, it is noted that Deisher apparently recognizes utility as a mitogen (proliferative) of cells of neuroectoderm origin, see in particular Background.

14. Any inquiry of a general nature or relating to the status of this general application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Papers relating to this application may be submitted to Technology Center 1600, Group 1640 by facsimile transmission. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). Should applicant wish to FAX a response, the current FAX number for Group 1600 is (703) 308-4242.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sharon L. Turner, Ph.D. whose telephone number is (703) 308-0056. The examiner can normally be reached on Monday-Friday from 8:00 AM to 4:30 PM. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Kunz, can be reached at (703) 308-4623.

Sharon L. Turner, Ph.D.
3/25/04

Gary L. Kunz

GARY KUNZ
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